FILE 'HOME' ENTERED AT 09:45:48 ON 01 APR 2003

=> file medline
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'MEDLINE' ENTERED AT 09:45:55 ON 01 APR 2003

FILE LAST UPDATED: 31 MAR 2003 (20030331/UP). FILE COVERS 1958 TO DATE.

On June 9, 2002, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/summ2003.html for a description on changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s conotoxin (p) disulfide (p) stability
          2531 CONOTOXIN
           415 CONOTOXINS
          2628 CONOTOXIN
                 (CONOTOXIN OR CONOTOXINS)
         22206 DISULFIDE
         10003 DISULFIDES
         26121 DISULFIDE
                 (DISULFIDE OR DISULFIDES)
        107537 STABILITY
          2435 STABILITIES
        108640 STABILITY
                 (STABILITY OR STABILITIES)
L1            7 CONOTOXIN (P) DISULFIDE (P) STABILITY

=> s l1 and py=1998
        445421 PY=1998
L2            2 L1 AND PY=1998

=> d l2 1-2 ibib abs

L2   ANSWER 1 OF 2     MEDLINE
ACCESSION NUMBER:    1998322088     MEDLINE
DOCUMENT NUMBER:     98322088   PubMed ID: 9657699
TITLE:               Roles of individual   ***disulfide***   bonds in the
                       ***stability***   and folding of an omega-  ***conotoxin***
                     .
AUTHOR:              Price-Carter M; Hull M S; Goldenberg D P
CORPORATE SOURCE:    Department of Biology, University of Utah, Salt Lake City
                     84112-0840, USA.
CONTRACT NUMBER:     5 P30 CA 42014 (NCI)
SOURCE:              BIOCHEMISTRY,   ***(1998 Jul 7)***   37 (27) 9851-61.
                     Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199807
ENTRY DATE:          Entered STN: 19980811
                     Last Updated on STN: 20000303
                     Entered Medline: 19980730
AB   Although it contains only 25 amino acid residues, omega-  ***conotoxin***
     MVIIA folds into a well-defined three-dimensional structure that is
     stabilized by 3   ***disulfide***   bonds. To assess the contributions of
     the   ***disulfides***   to folding and   ***stability***   , three
     analogues, each with one pair of   ***disulfide***   -bonded Cys residues
     replaced with Ala, were prepared and characterized. The analogues also
     contained a C-terminal Gly residue that is believed to be present when the
     peptide folds in vivo and has been shown previously to stabilize the
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native structure. Circular dichroism spectra and biological assays of the analogues indicated that removal of any one of the ***disulfide*** greatly destabilized the native conformation. The two ***disulfides*** in each analogue were also reduced much more rapidly than in the native form with three ***disulfides*** . When the analogues were fully reduced and allowed to form ***disulfides*** in the presence of oxidized and reduced glutathione, the native ***disulfides*** were not formed in preference to non-native ***disulfides*** , further indicating that the forms with two-native ***disulfides*** are not significantly stabilized by noncovalent interactions. However, the measured equilibrium constants for ***disulfide*** formation indicate that forming any two of the three native ***disulfides*** leads to an effective concentration of approximately 25-50 M for the two remaining thiols. The two- ***disulfide*** analogues thus appear to represent a stage of folding in which the polypeptide is constrained to a distribution of relatively compact conformations that greatly favor formation of the third ***disulfide*** and the final folded structure.

L2 ANSWER 2 OF 2 MEDLINE
ACCESSION NUMBER: 1998239743 MEDLINE
DOCUMENT NUMBER: 98239743 PubMed ID: 9571060
TITLE: Structure determination of the three ***disulfide*** bond isomers of alpha- ***conotoxin*** GI: a model for the role of ***disulfide*** bonds in structural ***stability*** .
AUTHOR: Gehrmann J; Alewood P F; Craik D J
CORPORATE SOURCE: Centre for Drug Design and Development, University of Queensland, Brisbane, QLD 4072, Australia.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, ***(1998 May 1)*** 278 (2) 401-15.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980713
Last Updated on STN: 19980713
Entered Medline: 19980630

AB The three possible ***disulfide*** bonded isomers of alpha- ***conotoxin*** GI have been selectively synthesised and their structures determined by 1H NMR spectroscopy. alpha- ***Conotoxin*** GI derives from the venom of Conus geographus and is a useful neuropharmacological tool as it selectively binds to the nicotinic acetylcholine receptor (nAChR), a ligand-gated ion channel involved in nerve signal transmission. The peptide has the sequence ECCNPACGRHYSC-NH2, and the three ***disulfide*** bonded isomers are referred to as GI(2-7;3-13), GI(2-13;3-7) and GI(2-3;7-13). The NMR structure for the native isomer GI(2-7;3-13) is of excellent quality, with a backbone pairwise RMSD of 0.16 A for a family of 35 structures, and comprises primarily a distorted 310 helix between residues 5 to 11. The two non-native isomers exhibit multiple conformers in solution, with the major populated forms being different in structure both from each other and from the native form. Structure-activity relationships for the native GI(2-7;3-13) as well as the role of the ***disulfide*** bonds on folding and ***stability*** of the three isomers are examined. It is concluded that the ***disulfide*** bonds in alpha- ***conotoxin*** GI play a crucial part in determining both the structure and ***stability*** of the peptide. A trend for increased conformational heterogeneity was observed in the order of GI(2-7;3-13)<GI(2-13;3-7)<GI(2-3;7-13). It was found that the peptide bond joining Cys2 to Cys3 in GI(2-3;7-13) is predominantly trans, rather than cis as theoretically predicted. These structural data are used to interpret the varying nAChR binding of the non-native forms.A model for the binding of native GI(2-7;3-13) to the mammalian nAChR is proposed, with an alpha-subunit binding face made up of Cys2, Asn4, Pro5, Ala6 and Cys7 and a selectivity face, comprised of Arg9 and His10. These two faces orient the molecule between the alpha and delta subunits of the receptor. The structure of the CCNPAC sequence of the native GI(2-7;3-13) is compared to the structure of the identical sequence from the toxic domain of heat-stable enterotoxins, which forms part of the receptor binding region of the enterotoxins, but which has a different ***disulfide*** connectivity.

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=> d his

     (FILE 'HOME' ENTERED AT 09:45:48 ON 01 APR 2003)

     FILE 'MEDLINE' ENTERED AT 09:45:55 ON 01 APR 2003
L1             7 S CONOTOXIN (P) DISULFIDE (P) STABILITY
L2             2 S L1 AND PY=1998

=> s conotoxin (p) disulfide
          2531 CONOTOXIN
           415 CONOTOXINS
          2628 CONOTOXIN
                 (CONOTOXIN OR CONOTOXINS)
         22206 DISULFIDE
         10003 DISULFIDES
         26121 DISULFIDE
                 (DISULFIDE OR DISULFIDES)
L3           121 CONOTOXIN (P) DISULFIDE

=> s l3 (p) (block? or protect?)
        339987 BLOCK?
        237584 PROTECT?
L4           49 L3 (P) (BLOCK? OR PROTECT?)

=> s l4 (p) N-termin?
        602335 N
        336187 TERMIN?
         57424 N-TERMIN?
                 (N(W)TERMIN?)
L5            5 L4 (P) N-TERMIN?

=> d l5 1-5 ibib abs

L5   ANSWER 1 OF 5     MEDLINE
ACCESSION NUMBER:    2000409250     MEDLINE
DOCUMENT NUMBER:     20320571   PubMed ID: 10861378
TITLE:               The cyclic contryphan motif CPxXPXC, a robust scaffold
                     potentially useful as an omega-conotoxin mimic.
AUTHOR:              Pallaghy P K; Norton R S
CORPORATE SOURCE:    Biomolecular Research Institute, 343 Royal Parade,
                     Parkville 3052, Australia.. Paul.Pallaghy@bioresi.com.au
SOURCE:              BIOPOLYMERS, (2000 Sep) 54 (3) 173-9.
                     Journal code: 0372525. ISSN: 0006-3525.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         200008
ENTRY DATE:          Entered STN: 20000907
                     Last Updated on STN: 20000907
                     Entered Medline: 20000828
AB   Contryphan-R, from venom of the cone-shell Conus radiatus, represents a
     novel cyclic peptide scaffold onto which residues may be grafted to mimic
     unrelated protein surfaces. Three substitutions were made at the x and X
     positions of the   ***disulfide***  -bridged motif CPxXPXC, where X and x
     represent any L- and D-handed residues, respectively, P represents proline
     or hydroxyproline, and C a half-cystine. These substitutions were designed
     to mimic part of the pharmacophore of the unrelated globular polypeptide
     omega-  ***conotoxin***   GVIA, which   ***blocks***   N-type calcium
     channels. The structure of this engineered contryphan, YNK-contryphan-R
     ([D-Tyr4, Asn5, Lys7]contryphan-R), is shown to be similar to that of
     native contryphan-R (Pallaghy et al., Biochemistry, 1999, Vol. 38, pp.
     13553-13559), confirming that the scaffold is robust with respect to the
     multiple substitutions. In particular, the alpha-beta bond vectors
     characterising the orientation of the side chains relative to the backbone
     are similar in contryphan-R, YNK-contryphan-R, and omega-  ***conotoxin***
     GVIA, which is the required result for a scaffold-based approach to
     molecular design. The solution structure of YNK-contryphan-R has an
       ***N***  -  ***terminal***  , nonhydrogen-bonded, chain reversal centered
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on Hyp3-D-Trp4, and a C-terminal type I beta-turn. A minor form due to cis-trans isomerism of the Hyp[redacted]ys3 peptide bond is present in YNK-contryphan-R in a larger proportion than in contryphan-R. It is evident, particularly from the (3)J(HalphaHN) coupling constants, that YNK-contryphan-R is more flexible than contryphan-R, probably due to the absence in YNK-contryphan-R of the Pro-Trp packing present in the native molecule. Nevertheless, the structure confirms that cyclic peptide molecular designs can achieve the intended conformations.

L5 ANSWER 2 OF 5 MEDLINE
ACCESSION NUMBER: 1999060038 MEDLINE
DOCUMENT NUMBER: 99060038 PubMed ID: 9843366
TITLE: Three-dimensional solution structure of alpha-conotoxin MII by NMR spectroscopy: effects of solution environment on helicity.
AUTHOR: Hill J M; Oomen C J; Miranda L P; Bingham J P; Alewood P F; Craik D J
CORPORATE SOURCE: Centre for Drug Design and Development, The University of Queensland, Brisbane, Australia.
SOURCE: BIOCHEMISTRY, (1998 Nov 10) 37 (45) 15621-30.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1MII
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981221

AB alpha- ***Conotoxin*** MII, a 16-residue polypeptide from the venom of the piscivorous cone snail Conus magus, is a potent and highly specific ***blocker*** of mammalian neuronal nicotinic acetylcholine receptors composed of alpha3 beta2 subunits. The role of this receptor type in the modulation of neurotransmitter release and its relevance to the problems of addiction and psychosis emphasize the importance of a structural understanding of the mode of interaction of MII with the alpha3 beta2 interface. Here we describe the three-dimensional solution structure of MII determined using 2D 1H NMR spectroscopy. Structural restraints consisting of 376 interproton distances inferred from NOEs and 12 dihedral restraints derived from spin-spin coupling constants were used as input for simulated annealing calculations and energy minimization in the program X-PLOR. The final set of 20 structures is exceptionally well-defined with mean pairwise rms differences over the whole molecule of 0.07 A for the backbone atoms and 0.34 A for all heavy atoms. MII adopts a compact structure incorporating a central segment of alpha-helix and beta-turns at the N- and C-termini. The molecule is stabilized by two ***disulfide*** bonds, which provide cross-links between the ***N*** - ***terminus*** and both the middle and C-terminus of the structure. The susceptibility of the structure to conformational change was examined using several different solvent conditions. While the global fold of MII remains the same, the structure is stabilized in a more hydrophobic environment provided by the addition of acetonitrile or trifluoroethanol to the aqueous solution. The distribution of amino acid side chains in MII creates distinct hydrophobic and polar patches on its surface that may be important for the specific interaction with the alpha3beta2 neuronal nAChR. A comparison of the structure of MII with other neuronal-specific alpha- ***conotoxins*** provides insights into their mode of interaction with these receptors.

L5 ANSWER 3 OF 5 MEDLINE
ACCESSION NUMBER: 1999036623 MEDLINE
DOCUMENT NUMBER: 99036623 PubMed ID: 9819194
TITLE: An O-glycosylated neuroexcitatory conus peptide.
AUTHOR: Craig A G; Zafaralla G; Cruz L J; Santos A D; Hillyard D R; Dykert J; Rivier J E; Gray W R; Imperial J; DelaCruz R G; Sporning A; Terlau H; West P J; Yoshikami D; Olivera B M
CORPORATE SOURCE: The Clayton Foundation Laboratories for Peptide Biology, The Salk Institute, San Diego, California 92186-5800, USA.
CONTRACT NUMBER: GM48677 (NIGMS)
SOURCE: BIOCHEMISTRY, (1998 Nov 17) 37 (46) 16019-25.

Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981217

AB We purified and characterized a novel peptide from the venom of the fish-hunting cone snail Conus striatus that inhibits voltage-gated K+ channels. The peptide, kappaA- ***conotoxin*** SIVA, causes characteristic spastic paralytic symptoms when injected into fish, and in frog nerve-muscle preparations exposed to the toxin, repetitive action potentials are seen in response to a single stimulus applied to the motor nerve. Other electrophysiological tests on diverse preparations provide evidence that is consistent with the peptide ***blocking*** K+ channels. The peptide has three ***disulfide*** bonds; the locations of Cys residues indicate that the spastic peptide may be the first and defining member of a new family of Conus peptides, the kappaA- ***conotoxins*** , which are structurally related to, but pharmacologically distinct from, the alphaA- ***conotoxins*** . This 30 AA tricyclic toxin has several characteristics not previously observed in Conus peptides. In addition to the distinctive biological and physiological activity, a novel biochemical feature is the unusually long linear ***N*** - ***terminal*** tail (11 residues) which contains one O-glycosylated serine at position 7. This is the first evidence for O-glycosylation as a posttranslational modification in a biologically active Conus peptide.

L5 ANSWER 4 OF 5 MEDLINE
ACCESSION NUMBER: 94321097 MEDLINE
DOCUMENT NUMBER: 94321097 PubMed ID: 8045682
TITLE: Synthesis of disulfide-bridged fragments of omega-conotoxins GVIA and MVIIA. Use of Npys as a protecting/activating group for cysteine in Fmoc syntheses.
AUTHOR: Simmonds R G; Tupper D E; Harris J R
CORPORATE SOURCE: Lilly Research Centre Ltd., Eli Lilly & Co., Windlesham, Surrey, UK.
SOURCE: INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, (1994 Apr) 43 (4) 363-6.
Journal code: 0330420. ISSN: 0367-8377.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940909
Last Updated on STN: 20000303
Entered Medline: 19940830

AB The 3-nitro-2-pyridinesulphenyl (Npys) moiety is finding increasing utility as a ***protecting*** -activating group for cysteine, particularly in the synthesis of cyclic and unsymmetrical ***disulfides*** using the Boc strategy. This chemistry has been extended to peptides assembled by the Fmoc strategy. ***N*** - ***Terminal*** Cys(Npys) is introduced via Boc-Cys(Npys)-OPfp. Non- ***N*** - ***terminal*** Cys(Npys) is incorporated by reacting a resin-bound, fully ***protected*** Cys(Acm) peptide with NpysCl. This approach has been applied to the synthesis of four ***disulfide*** -bridged fragments of omega- ***conotoxins*** GVIA and MVIIA.

L5 ANSWER 5 OF 5 MEDLINE
ACCESSION NUMBER: 94047089 MEDLINE
DOCUMENT NUMBER: 94047089 PubMed ID: 8230223
TITLE: Three-dimensional structure in solution of the calcium channel blocker omega-conotoxin.
AUTHOR: Pallaghy P K; Duggan B M; Pennington M W; Norton R S
CORPORATE SOURCE: NMR Laboratory, Biomolecular Research Institute, Parkville, Australia.
SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1993 Nov 20) 234 (2) 405-20.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199312
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 20000303
Entered Medline: 19931215

AB The 27 amino acid residue polypeptide omega- ***conotoxin*** GVIA, from venom of the cone shell Conus geographus, ***blocks*** neuronal voltage-activated calcium channels at picomolar concentrations. The three-dimensional structure in aqueous solution of synthetic omega- ***conotoxin*** has been determined from two-dimensional 1H n.m.r. data recorded at 600 MHz. Structural constraints consisting of interproton distances inferred from NOEs and dihedral angles from spin-spin coupling constants were used as input for distance geometry calculations with the program DSPACE. The structures were then refined using back-calculation of NOESY spectra. The family of structures obtained in this way is well defined by the n.m.r. data, the best 12 structures having pairwise root-mean-square differences of 0.68 (+/- 0.15) A over the backbone heavy atoms (N, C alpha and C) and 1.15 (+/- 0.17) A over all heavy-atoms. The molecule adopts a compact structure consisting of a small, triple-stranded, anti-parallel beta-sheet and several reverse turns. All three tyrosine residues are located on the molecular surface, which is noteworthy for its abundance of side-chain hydroxyl groups. There is no negatively charged group in ***conotoxin*** , but the five positively charged groups are distributed in three small patches on the surface, one of which, made up of the ammonium moieties of the ***N*** ***terminus*** and Lys2, may contribute to the receptor-binding surface of the molecule. An isomer of ***conotoxin*** with the same amino acid sequence, but different ***disulfide*** pairings, has also been investigated. Its structure is less well ordered than that of native ***conotoxin*** and it shows significant heterogeneity, probably as a result of cis-trans isomerism preceding hydroxyproline residues.

=> d his

(FILE 'HOME' ENTERED AT 09:45:48 ON 01 APR 2003)

FILE 'MEDLINE' ENTERED AT 09:45:55 ON 01 APR 2003
L1 7 S CONOTOXIN (P) DISULFIDE (P) STABILITY
L2 2 S L1 AND PY=1998
L3 121 S CONOTOXIN (P) DISULFIDE
L4 49 S L3 (P) (BLOCK? OR PROTECT?)
L5 5 S L4 (P) N-TERMIN?

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.89	5.10

STN INTERNATIONAL LOGOFF AT 09:51:28 ON 01 APR 2003